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A pipeline for the analysis of 18F-FDG PET data on the cortical surface and its evaluation on ADNI

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Background: 18F-fluorodeoxyglucose (FDG) PET reflects glucose consumption, which correlates with the activity of the synapses in the cortex. FDG PET can thus be used as a marker of synaptic dysfunction when diagnosing neurodegenerative diseases such as Alzheimer's disease (AD). Surface-based analysis is well suited to study properties of the cortex and has been widely used for cortical thickness analysis (Tustison et al. 2014). FreeSurfer 6 has recently been released, providing tools for partial volume correction (PVC) and projection of signals onto surfaces. However, these functionalities are not straightforward to use. We aim at mitigating these limitations and present a fully automated pipeline for the analysis of FDG PET data on the cortical surface, both in the subject's space and in a common template, enabling surface-based analysis of PET data on large datasets, through a non-trivial combination of different tools.

Methods: Our pipeline is composed of i) co-registration of PET and T1-w MRI (T1) images, ii) SUVR normalization, iii) PVC, iv) robust projection of the PET signal onto the subject's cortical surface, v) spatial normalization to a template. Note that it requires having run beforehand the recon-all pipeline of FreeSurfer.

First i) the subject's PET is registered to the T1 using *spmregister* (FreeSurfer). ii) The PET image is normalized using the pons from the Pick atlas in MNI space as reference region. Registration to MNI space is performed using SPM12. iii) PVC is performed to limit the spill-out of activity outside of the cortex using the iterative Yang algorithm (PETPVC) (Thomas et al. 2016) with regions obtained from *gtmseg* (FreeSurfer). iv) Based on the subject's white surface and cortical thickness, 7 surfaces for each hemisphere are computed, ranging from 35% to 65% of the grey matter thickness. Each surface has the same number of vertices, allowing the matching of the same vertex across the thickness. The partial volume corrected data are projected onto these meshes and the 7 values are averaged, giving more weight to the vertices near the center of the cortex as they have a higher probability of intersecting the signal. v) We resample the obtained data into a common template (FsAverage from FreeSurfer) for subsequent analysis. This pipeline has been integrated into Clinica, a software platform for neuroscience studies available at www.clinica.run, and will be released at the time of the conference.

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Results: To assess the value of the method, we applied it to 116 cognitively normal amyloid negative subjects (CN) and 126 amyloid positive subjects with AD from the Alzheimer's Disease Neuroimaging Initiative (ADNI) study. A subset of 30 CN and 30 AD subjects was also studied. Examples of PET projections are shown in Fig 1.

When performing group comparison, we compared the proposed surface-based approach to a standard voxel-based approach, whose results were projected onto the cortical surface. No matter the number of subjects considered, both approaches identified the areas where hypometabolism is expected (Herholz et al., 2002), i.e. frontal, temporal and parietal lobes, and posterior cingulate cortex (Fig 2), and they were more clearly defined with the proposed surface-based approach.

We also used the vertices as features to feed a linear SVM classifier, and assessed the classification performance when differentiating CN and AD subjects. A balanced accuracy of 91.5% was reached, performing equally as well as a linear SVM with voxel-based features (91.3%).

Conclusion: We introduced a robust and automatic pipeline to project the FDG PET signal onto the cortical surface and applied it to a large number of ADNI subjects. We showed that the proposed surface-based approach was able to identify areas where hypometabolism is expected when studying AD as well as a standard volume-based approach. The method can be used both for visualization and data analysis purposes.

References:

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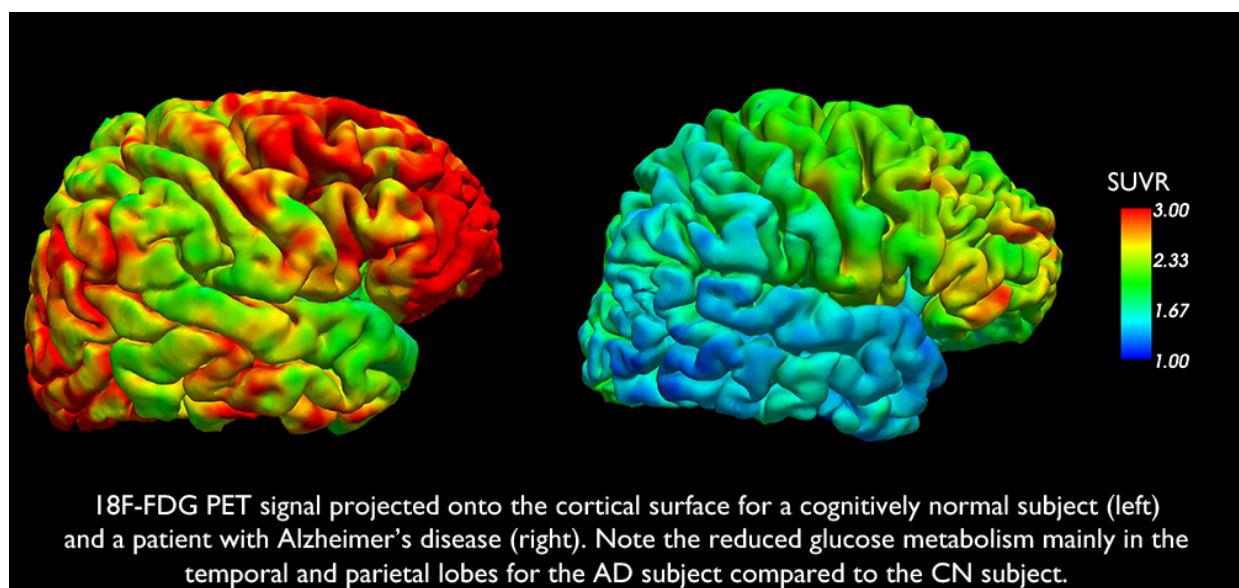
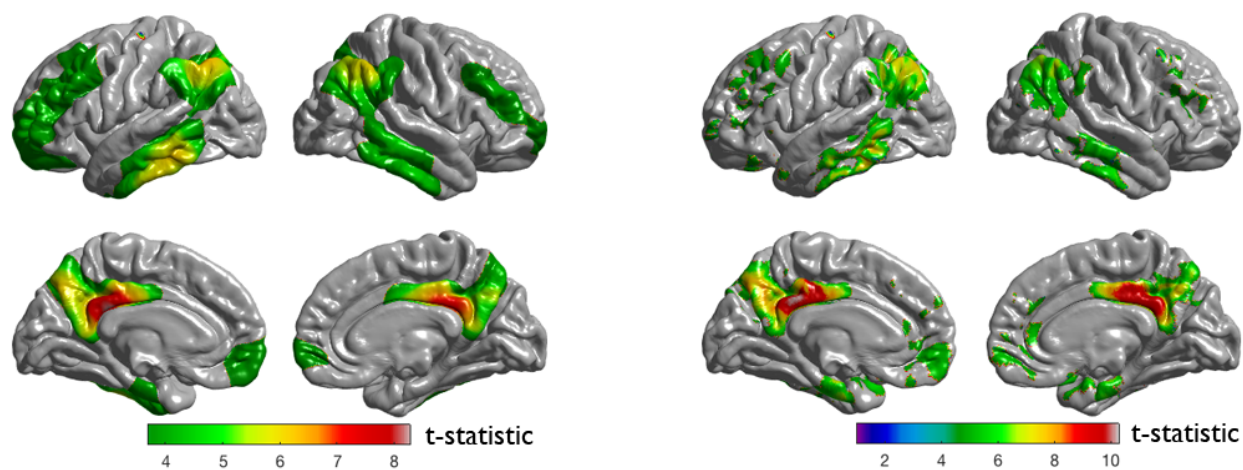


Figure 1



Results of the surface-based group comparison (left) and volume-based group comparison subsequently projected onto the cortical surface (right) of 30 CN with negative amyloid status and 30 AD with positive amyloid status from ADNI, using sex and age as covariates. The t-statistic was thresholded to only show areas corresponding to a p-value smaller than 0.05.

Figure 2